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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/707,994	01/30/2004	Roger Ariel Alberto	1292.1	1993

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/707,994	ALBERTO ET AL.	
	Examiner	Art Unit	
	BRANDON J. FETTEROLF	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/26/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to the Amendment

The Amendment filed on 12/26/2007 in response to the previous Non-Final Office Action (8/31/2007) is acknowledged and has been entered.

Claims 22-53 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 12/26/2007 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Rejections Withdrawn:

The rejection of Claims 51-53 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicants amendments to remove the limitation "chemical moiety".

The rejection of Claims 22-24, 26-29, 32-37 and 40-53 under 35 U.S.C. 102(b) as being anticipated by Toner et al. (W0 93/21957, 1993, IDS, of record) as evidenced by Albert et al. (US 5,776,894, 1998, of record) is withdrawn in view of Applicants arguments and amendments. In particular, Toner et al. does not teach that the derivative of phenanthroline comprises at least one unsubstituted aromatic ring that shares two carbons with only one other aromatic ring.

As such, all other rejections using in combination the Toner et al. reference are withdrawn.

The rejection of Claims 22 and 32 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,844,425 is withdrawn in view of Applicants filing of a Terminal Disclaimer.

Rejections Maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-39, 43-48 and 50 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter.

The phase "intercalating moiety is configured to insert into the structure of deoxyribonucleic acid" recited in claims 22 and 32 is a relative term which renders the claim indefinite. The phase "intercalating moiety is configured to insert into the structure of deoxyribonucleic acid" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instant case, it is unclear what is encompassed by the phrase "intercalating moiety is configured to insert into the structure of deoxyribonucleic acid". For example, configuring the intercalating moiety to insert into the structure of deoxyribonucleic acid can be reasonably interpreted as by the "hand of man", wherein the intercalating moiety if configured as a salt or designed synthetically so as to insert into the structure of deoxyribonucleic acid. Alternatively, configuring the intercalating moiety to insert into the structure of deoxyribonucleic acid can be reasonably interpreted as the intercalating moiety itself being configured to insert into the structure of deoxyribonucleic acid such as the intercalating moiety being planar and heterocyclic aromatic. For examination purposes, the phase "intercalating moiety is configured to insert into the structure of deoxyribonucleic acid" will be interpreted as intercalating moiety itself being configured to insert being capable of inserting into the structure of deoxyribonucleic acid such as the intercalating moiety being planar and heterocyclic aromatic, e.g. a structural property of the intercalating moiety.

In response to this rejection, Applicants assert that as stated in Barton, "DNA binding agents tend to interact noncovalently with the host molecule through two general modes... (ii) through an intercalative association in which a planar, hetero-aromatic moiety slides between teh base pairs." Barton p. 271. Moreover, Applicants assert that the authors point out that "[s]ince its proposal by Lerman in 1961 as a mode of DNA binding by planar aromatic molecules, the physical effects and characteristics of intercalation on DNA structure have been well studies." Accordingly, Applicants assert that one or ordinary skill in the art would understand the term "intercalating moiety" and, thus, the scope of the claims as written. Moreover, Applicants assert that the amended claims recite structural details of the intercalating moiety. As such, Applicants contend that this limitation specifically refers to an intercalating moiety having a single, unsubstituted aromatic ring

fused to only one other aromatic ring which is capable of inserting between the base pairs of a DNA sequence; and therefore, adequately clarifies the phrase "configured to insert into the structure of deoxyribonucleic acid" as recited by claims 22 and 32.

These arguments have been carefully considered, but are not found persuasive.

In the instant case, the Examiner acknowledges and does not dispute Applicants assertions that the phrase intercalating moiety would have been understood by one of ordinary skill in the art at the time of filing. However, the Examiner recognizes that while Applicants have amended the claims to recite structural limitations, it is unclear how the structural limitations further clarify the limitation of configuring to insert into the structure of deoxyribonucleic acid. As noted above, configuring the intercalating moiety to insert into the structure of deoxyribonucleic acid can be reasonably interpreted as by the "hand of man", wherein the intercalating moiety if configured as a salt or designed synthetically so as to insert into the structure of deoxyribonucleic acid. Alternatively, configuring the intercalating moiety to insert into the structure of deoxyribonucleic acid can be reasonably interpreted as the intercalating moiety itself being configured to insert into the structure of deoxyribonucleic acid such as the intercalating moiety being planar and heterocyclic aromatic. For examination purposes, the phase "intercalating moiety is configured to insert into the structure of deoxyribonucleic acid" will be interpreted as intercalating moiety itself being configured to insert being capable of inserting into the structure of deoxyribonucleic acid such as the intercalating moiety being planar and heterocyclic aromatic, e.g. a structural property of the intercalating moiety.

New Rejections Necessitated by Amendment:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 22-29, 32-37 and 40-53 are rejected under 35 U.S.C. 102(e) as being anticipated by Mattes (US 5,759,514, 1994).

Mattes teaches a conjugate comprising a tumor targeting protein or polypeptide linked to a radiolabeled nucleic acid-targeting small molecule, wherein the small molecule, after being liberated from the targeting protein by intracellular enzymes endogenous to the targeted tumor cell, is capable of passing through the lysosomal and nuclear membranes and intercalating a nuclear component (column 1, lines 49-56). With regards to the tumor targeting protein, the patent teaches that tumor targeting proteins include, but are not limited to, antibodies (column 2, lines 63-66). With regards to the nucleic acid small molecule, the patent teaches that nucleic acid small molecules include, but are not limited to, acridine and derivatives thereof, as well as phenanthridines (column 2, liens 41-61). With regards to the radiolabel, the patent teaches that the radiolabels include, but are not limited to, ^{188}Rh (column 2, line 40). Moreover, the patent teaches a method of treating a patient having a tumor comprising the step of administering to the patient a therapeutically effective amount of the aforementioned therapeutic anti-tumor conjugate (column 2, lines 13-16).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30-31 and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mattes (US 5,759,514, 1994), as applied to claims 22-29, 32-37 and 40-53 above, in view of Holley et al. (Cancer Research 1992; 52: 4190-4195, of record).

Mattes teaches a conjugate comprising a tumor targeting protein or polypeptide linked to a radiolabeled nucleic acid-targeting small molecule, wherein the small molecule, after being liberated from the targeting protein by intracellular enzymes endogenous to the targeted tumor cell, is capable of passing through the lysosomal and nuclear membranes and intercalating a nuclear component

(column 1, lines 49-56). With regards to the tumor targeting protein, the patent teaches that tumor targeting proteins include, but are not limited to, antibodies (column 2, lines 63-66). With regards to the nucleic acid small molecule, the patent teaches that nucleic acid small molecules include, but are not limited to, acridine and derivatives thereof, as well as phenanthridines (column 2, liens 41-61). With regards to the radiolabel, the patent teaches that the radiolabels include, but are not limited to, ^{188}Rh (column 2, line 40). Moreover, the patent teaches a method of treating a patient having a tumor comprising the step of administering to the patient a therapeutically effective amount of the aforementioned therapeutic anti-tumor conjugate (column 2, lines 13-16).

Mattes does not explicitly teach that tumor seeking molecule is spermidine.

Holley et al. teach a method of targeting chlorambucin to a tumor cell by conjugating chlorambucin to spermidine (page 4191, 1st column, 1st full paragraph). In particular, the reference teaches that the chlorambucin-spermidine conjugate showed greater anti-tumor activity both in vivo and in vitro compared to chlorambucin due to increased tumor uptake and increased affinity for DNA (page 4194, 2nd column, last paragraph)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the conjugate taught by Mattes. with a spermidine in view of the teachings Holley et al.. One would have been motivated to so because Holley et al. teach that spermidine conjugates show increase tumor uptake and increased affinity for DNA. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by modifying the conjugate taught by Mattes with a spermidine in view of the teachings Holley et al, one would achieve a targeted radioactive immunoreagent for the treatment and diagnosis of a tumor.

Conclusion

Therefore, No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the

THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRANDON J. FETTEROLF whose telephone number is (571)272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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